

CLAIMS

1. A bovine comprising a non-naturally occurring mutation in one or both alleles of an endogenous prion nucleic acid
2. The bovine of claim 1, wherein said mutation reduces the expression of functional prion protein.
3. The bovine of claim 2, wherein said mutation substantially eliminates the expression of functional prion protein.
4. The bovine of claim 1, wherein said mutation is hemizygous.
5. The bovine of claim 1, wherein said mutation is homozygous.
6. The bovine of claim 1, wherein said mutation comprises an insertion of a positive selection marker into a prion nucleic acid.
7. The bovine of claim 1, wherein said mutation comprises an insertion of a STOP codon into a prion nucleic acid.
8. The bovine of claim 1, wherein said mutation comprises a deletion of one or more nucleotides in a prion nucleic acid.
9. The bovine of claim 1, comprising one or more nucleic acids comprising one or more transgenes and expressing an mRNA or protein encoded by said transgene(s).
10. The bovine of claim 1, comprising one or more nucleic acids comprising all or part of a xenogenous immunoglobulin (Ig) gene which undergoes rearrangement and expresses more than one xenogenous Ig molecule.

11. The bovine of claim 10, comprising one or more nucleic acids encoding a xenogenous antibody.

12. The bovine of claim 11, wherein said xenogenous antibody is a human antibody.

13. The bovine of claim 12, wherein said antibody is expressed in serum and/or milk.

14. The bovine of claim 1, comprising a mutation that reduces the expression of an endogenous antibody.

15. The bovine of claim 14, wherein said mutation reduces the expression of functional IgM heavy chain.

16. The bovine of claim 15, wherein said mutation substantially eliminates the expression of functional IgM heavy chain.

17. The bovine of claim 14, wherein said mutation reduces the expression of functional Ig light chain.

18. The bovine of claim 17, wherein said mutation substantially eliminates the expression of functional Ig light chain.

19. The bovine of claim 14, wherein said mutation reduces the expression of functional IgM heavy chain and functional Ig light chain.

20. The bovine of claim 19, wherein said mutation substantially eliminates the expression of functional IgM heavy chain and functional Ig light chain.

21. The bovine of claim 1, comprising a mutation in one or both alleles of

an endogenous nucleic acid encoding alpha-(1,3)-galactosyltransferase.

22. The bovine of claim 1, comprising a mutation in one or both alleles of an endogenous nucleic acid encoding J chain.

23. The bovine of claim 1, comprising a nucleic acid encoding an exogenous J chain.

24. The bovine of claim 23, wherein said J chain is a human J chain.

25. A bovine cell comprising a non-naturally occurring mutation in one or both alleles of an endogenous prion nucleic acid.

26. The cell of claim 25, wherein said mutation reduces the expression of functional prion protein.

27. The cell of claim 26, wherein said mutation substantially eliminates the expression of functional prion protein.

28. The cell of claim 25, wherein said mutation is hemizygous.

29. The cell of claim 25, wherein said mutation is homozygous.

30. The cell of claim 25, wherein said cell is a fetal fibroblast.

31. The cell of claim 25, wherein said cell is a B-cell.

32. A method for producing a transgenic bovine cell having reduced expression of functional prion protein, comprising introducing a first prion gene targeting vector into a bovine cell under conditions that allow homologous

recombination between said first vector and a first allele of an endogenous prion nucleic acid in said cell, thereby introducing a hemizygous mutation in said cell.

33. The method of claim 32, further comprising introducing said first vector into said cell under conditions that allow homologous recombination between said first vector and a second allele of an endogenous prion nucleic acid in said cell, thereby introducing homozygous mutation in said cell.

34. The method of claim 32, further comprising introducing a second prion gene targeting vector that has a different antibiotic resistance gene than said first vector into said cell under conditions that allow homologous recombination between said second vector and a second allele of an endogenous prion nucleic acid in said cell, thereby introducing a homozygous mutation in said cell.

35. The method of claim 32, wherein said cell is a bovine fibroblast.

36. The method of claim 35, wherein said cell is a bovine fetal fibroblast.

37. A method for producing a transgenic bovine having reduced expression of functional prion protein, said method comprising the steps of:

(a) inserting a cell, a chromatin mass from a cell, or a nucleus from a cell into an oocyte, wherein said cell comprises a first mutation in an endogenous prion nucleic acid; and

(b) transferring said oocyte or an embryo formed from said oocyte into the uterus of a host bovine under conditions that allow said oocyte or said embryo to develop into a fetus.

38. The method of claim 37, wherein said fetus develops into a viable offspring.